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Case Reports

Recurrence of myopericarditis following mRNA COVID-19 vaccination in a male adolescent

Short title: Myocarditis recurrence after COVID-19 vaccine

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Brief Summary

We present a case of recurrent myopericarditis in a young man following an initial episode of influenza virus-induced myopericarditis after receiving the mRNA-1273 COVID-19 vaccine. This case highlights the importance of assessing patients' backgrounds, which may help elucidate the mechanism and risk factors of vaccine-induced myopericarditis.

Abstract

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). It has spread worldwide, resulting in health and economic crises. Vaccination against SARS-CoV-2 infection is considered a valid prevention measure to control this pandemic. There have been reports of cases of myopericarditis following mRNA COVID-19 vaccination. We present a case of a 20-year-old man with recurrent myopericarditis following an initial episode of influenza virus-induced myopericarditis and after receiving a second dose of the mRNA-1273 Moderna COVID-19 vaccine. Careful attention should be paid to patients with a history of myocarditis following COVID-19 vaccination.

Introduction

Coronavirus disease 2019 (COVID-19) is caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) that has spread worldwide, resulting in health and economic crises. Vaccination against SARS-CoV-2 is considered a protective approach with more than 95% efficacy to control the COVID-19 pandemic [1]. However, some cases of myopericarditis have recently been reported as complications of mRNA COVID-19 vaccination with an incidence of 1 case per 10,000–100,000 inoculations [2]. Although these events are rare, cases were much more common following a second dose, especially in young male adolescents [2]. Herein, we present a case of a 20-year-old male adolescent with recurrent acute myopericarditis five years after an initial episode of acute influenza virus-induced myopericarditis and two days after receiving a second dose of the mRNA-1273 Moderna COVID-19 vaccine.

Case

A 20-year-old male adolescent had a history of seasonal influenza virus-induced myopericarditis in 2016 (data not shown). He presented to our hospital in July 2021 with chief complaints of fever and severe sharp chest pain in deep breathing improved by sitting up. The patient had been well and free from any flu-like illnesses a couple of months before admission. Two days before admission, he received a second dose of the mRNA-1273 Moderna COVID-19 vaccine. Initial vital signs were normal, except for a high body temperature of 38.8□. Electrocardiography (ECG) showed global ST–T wave elevation (**Figure 1A**). Transthoracic echocardiography revealed regional hypokinesis of

the anteroseptal wall, an ejection fraction of 53.8%, and no pericardial effusion (**Supplemental Movie 1A**). Serum creatinine kinase (CK) and troponin T levels were elevated. Polymerase chain reaction testing for SARS-CoV-2 and antigen tests for influenza virus were negative. Paired serum samples were negative for viruses that were possible causes of myocarditis, including coxsackievirus, adenovirus, and human parvovirus B19. Accordingly, the patient received conservative management, including administration of oral loxoprofen at 160 mg/day for one week. Serum CK (1190 IU/L) and troponin T (0.710 ng/mL) levels peaked on day 2 after admission. Cardiac magnetic resonance imaging (cMR) showed no apparent findings on T1 and T2 mapping. However, high signal intensity on T2-weighted in the inferolateral wall in regions with late gadolinium enhancement was suggestive of acute myocarditis (**Figure 2A and 2B**). Changes in ECG findings revealed a pseudonormalized ST–T pattern followed by T-wave inversion in precordial leads (**Figure 1B and 1C**). His symptoms gradually resolved, and he was discharged on day 5. He remained stable and his left ventricular function improved one month after discharge (**Supplemental Movie 1B**).

Discussion

Vaccination against SARS-CoV-2 is considered a potent approach to control the COVID-19 pandemic. The efficacy of the mRNA COVID-19 vaccine has been reported to be 95% [1]. However, some cases of myopericarditis have recently been reported as complications of mRNA COVID-19 vaccination with an incidence of 1 case per 10,000–100,000 inoculations [2]. Although these events are as rare as extrapulmonary manifestations of influenza, cases were much more common following a second dose of mRNA COVID-

19 vaccination, especially in young male adolescents [2].

Historically, vaccine-induced myopericarditis was reported as rare adverse events, such as after receiving smallpox or influenza virus vaccinations [3]. Circulating heart-reactive autoantibodies have been reported in a high percentage of patients with myocarditis and have been linked to its pathogenesis. Another possible mechanism for vaccine-induced myocarditis might have been molecular similarities between anti-virus antibodies and self-antigens. The mRNA-1273 vaccine is a lipid nanoparticle-encapsulated mRNA-based vaccine that encodes the prefusion-stabilized full-length spike protein of SARS-CoV-2. Of note, antibodies against SARS-CoV-2 spike proteins have been experimentally shown to cross-react with structurally similar human peptide sequences, including alpha-myosin [4]. In addition, a history of infection can be related to the magnitude of immune response to the current infection in a phenomenon referred to as “original antigenic sin”. A case of repeated pericarditis after vaccination for influenza has been reported [5]. This concept refers to cross-reacting immunity due to past infections with similar virus strains, which must be considered when interpreting immune responses to infections and vaccinations. However, there have been some reports that common viruses including influenza virus were poor sources of cross-reactive immunity to SARS-CoV-2 [6]. Since we did not perform testing for viral genomes or autoantibodies in heart tissues, a direct relationship between influenza virus-induce and COVID-19 mRNA vaccine-induced myocarditis cannot be definitively established. In the setting of stable uncomplicated myocarditis, cMR rather than endomyocardial biopsy is recommended. However, biopsy would be further considered for elucidating the mechanism [7].

COVID-19 has spread worldwide and vaccination against COVID-19 is an effective

approach to prevent infection and aggravation. There have been some reports of myocarditis induced by COVID-19 mRNA vaccine. However, the exact mechanism of mRNA vaccine-induced myocarditis has yet to be determined. Our case was a patient with recurrent myocarditis following an initial episode of influenza infection and after receiving the mRNA-1273 Moderna COVID-19 vaccine. It is not that COVID-19 vaccination is not recommended for patients with prior myocarditis. However, careful watch would be considered. Accumulation of myopericarditis cases following mRNA vaccination, and assessing their backgrounds, particularly regarding the immune system, may help elucidate the mechanism and risk factors for developing this adverse event.

Novel teaching points

□Both influenza myocarditis and COVID-19 mRNA vaccine-induced myocarditis are rare but might occur consecutively.

□Careful watch is important after COVID-19 vaccination for cases with a history of myocarditis.

Conclusion

We experienced a case of a 20-year-old man with recurrent myopericarditis following an initial episode of influenza virus-induced myopericarditis and after receiving a

second dose of the mRNA-1273 Moderna COVID-19 vaccine. Careful watch should be considered after COVID-19 vaccination for cases with a history of myocarditis.

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Disclosures

None.

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Figure Legends

Figure 1. ECG changes during hospitalization and after discharge.

ECG obtained upon admission showing global ST-T wave elevation (A). Changes in ECG reveals an improved ST-T elevation on day 2 (B), followed by T–wave inversion in precordial leads one month after discharge (C). *ECG, electrocardiogram.*

Figure 2. cMR imaging on day 3.

cMR imaging shows regional hyperintensity on T2-weighted (A) and linear sub-epicardial LGE (B) in the inferolateral wall. *cMR, cardiac magnetic resonance; LGE, late gadolinium enhancement.*

Supplemental Video 1. 2D speckle tracking echocardiography.

TTE performed on admission day shows hypokinesis of the anteroseptal wall with no pericardial effusion (A). TTE findings one month after discharge shows an almost normal left ventricular function (B). *2D, 2-dimensional; TTE, transthoracic echocardiography.*